

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

IN RE: MARSHALL, WILLIAM E.)	
)	APPEAL NO. _____
SERIAL NO: 09/883,550)	
)	
FOR: METHODS AND COMPOSITIONS FOR MODULATING IMMUNE SYSTEMS OF ANIMALS)	BRIEF ON APPEAL
)	
FILED: JUNE 18, 2001)	
)	
)	
GROUP ART UNIT: 1638)	

To Commissioner for Patents
Mail Stop Appeal Brief – Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sirs and Madams:

In response to the Notification of Non-Compliant Appeal Brief dated December 5, 2006, please find attached a revised summary of the claimed matter for the above-identified appeal brief. Applicants believe that they are in compliance with 37 CFR 41.37(c)(1)(v) and request that this be entered.

=====

CERTIFICATE OF MAILING/TRANSMISSION

I hereby certify that this correspondence is, on the date shown below, being:

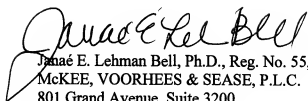
EXPRESS MAILING
☐ deposited with the United States Postal Service with sufficient postage as Express mail in an envelope addressed to the Commissioner for Patents, Mail Stop BPAI - Supplemental Appeal Brief P.O. Box 1450, Alexandria, VA 22313-1450 Express Label No. _____

ELECTRONIC
☒ transmitted by electronic to the Patent and Trademark Office, using the EFS

Date: 1-4-07


JANA E. LEHMAN BELL, Ph.D.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "J. E. Lehman Bell". The signature is fluid and cursive, with the first name "J" being particularly large and stylized.

J. E. Lehman Bell, Ph.D., Reg. No. 55,370
McKEE, VOORHEES & SEASE, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No. (515) 288-3667
Fax No. (515) 288-1338

Attorneys of Record

- pw -

V. SUMMARY OF CLAIMED SUBJECT MATTER

This invention relates to methods and compositions for modulating immune responses of animals or humans. (*See* Original specification as filed, p. 9, ll. 15-34, and p. 10, ll. 1-19). More particularly, the invention relates to methods of modulating immune responses of animals or humans by administering effective amounts of a partially purified composition prepared from a mixture released by the stressing of bacteria after they have been grown under specified conditions. (*See* Original specification as filed, p. 11, l. 6 – p. 12, l. 28; p. 21, l. 1 – p. 22, l. 12). This composition includes stress response factors that activate and modulate circulating macrophages. (*See* Original specification as filed, p. 1, ll. 27-33; p. 19, l. 1 – p. 20, l. 20).

The present inventors have found that the stress-response-factors (SRFs), between 0.5 and 10. kDa are a rich new source of natural, normally-occurring, co-evolutionarily evolved immune modulators that can be safely used to protect animals and humans from infections and over-stimulation of their immune system. (*See* Original specification as filed, p. 21, l. 1– p.22, l. 14).

The present inventor has discovered that SRFs that modulate the immune system may be created by growing bacteria in a medium and exposing said bacteria to biological, chemical or physical stress for at least two or more sequential periods of stress of approximately 20 minutes or less. (*See* Original specification as filed, p. 11, l. 6 – p. 12, l. 28). The inventor has discovered that the bacteria after such stressing release a stress response product comprising stress response factors (SRFs) into the medium. (*See* Original specification as filed, p. 12, ll. 10-28). These SRFs are then separated from the medium to form a separated product. (*See* Original specification as filed, p. 12, l. 29 – p.

13, l. 4). The separated product is then filtered to remove substances having a molecular weight of greater than 10kDa to form a filtrate. (See Original specification as filed, p. 12, l. 29 – p. 13, l. 4). The resulting filtrate of less than 10kDa can then be administered to animals. (See Original specification as filed, p. 13, l. 34 – p. 14, l. 3).

This fraction was shown in cell cultures to induce the release of cytokines, IL-1, IL-6, and TNF α and decrease the expression of individual surface receptors CD-14 and CD-16 on macrophages, thereby re-centering a dysfunctional immune system and desensitizing it to a subsequent lethal challenge of injected endotoxin, LPS. (See Original specification as filed, p. 19, l. 1 – p. 22, l. 14). Furthermore, in vitro testing indicates their potential role as adjuvants by stimulating the release of IL-12. (See Original specification as filed, p. 5, ll. 13-15).

An additional discovery is the finding that feral colonies of bacteria yield more oligomeric SRFs than non-feral or laboratory strains. (See Original specification as filed, p. 5, ll. 15-18). However, after stressing, laboratory strains assume the more robust growth characteristics of feral strains and the subsequent release of more SRFs when stressed. (See Original specification as filed, p. 5, ll. 19-22). The release of SRFs can be tracked by measuring their peak of absorption at 254 nm that typically is associated with nucleotides. (See Original specification as filed, p. 16, l. 23 – p. 17, l. 14, p. 12, ll. 29-31).

The discovery of the release of immune-activating and modulating factors has broad implications to improving the immune response through diets and pharmaceutical preparations for humans and animals. (See Original specification as filed, p. 5, ll. 23-26). Products, e.g. milk, cheese, yogurts contain viable bacteria, which, when transferred to the nutrient deprived and pH neutral environment of the mouth release SRFs. (See

Original specification as filed, p. 5, ll. 26-28). If such products were formulated to extend the dwell-time in the mouth, more SRFs would be released, activating and modulating a greater local immune response. (*See* Original specification as filed, p. 5, ll. 29-31). Material relevant to the appealed claims is described throughout the Specification.